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10/679,123	10/03/2003	Bernd Klinksiek	Bayer 10261-WCG	2253
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GERSTENZANG, WILLIAM C.			EXAMINER	MAEWALL, SNICDHHA
NORRIS MC LAUGHLIN & MARCUS, PA			ART UNIT	PAPER NUMBER
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NEW YORK, NY 10022				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/679,123	Applicant(s) KLINKSIEK ET AL.
	Examiner Snigdha Maewall	Art Unit 1612

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 16 March 2010.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-40,42,44 and 45 is/are pending in the application.

4a) Of the above claim(s) 1-15 and 37-39 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 16-36,40,42,44 and 45 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)
 Paper No(s)/Mail Date _____

4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date _____

5) Notice of Informal Patent Application

6) Other: _____

DETAILED ACTION

Summary

1. Receipt of Applicants arguments/remarks, amended claims filed on 03/16/10 is acknowledged.

Claims 1-15, 37-39 remain withdrawn. Claims 41 and 43 have been cancelled.

Claims **16-36, 40, 42 and 44-45** are under prosecution.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims **16-36, 40, 42 and 44-45** are rejected under 35 U.S.C. 103(a) as being unpatentable over Irvin et al. (USP 7,276,184) in view of Westesen et al. (US Patent No. 5,885,486).

Irvin et al. teaches preparation of nanoscale particulate material comprising functional materials which are solids at ambient temperature in conjunction with a

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surfactant/dispersant material within a carrier fluid carbon dioxide which is a compressed gas or supercritical fluid phase, depressurization of this mixture results in evaporation of carrier fluid which is carbon dioxide in this case and resulting in formation of nanoscale particles, see column 5, lines 10-25. The temperature used is from range of zero to hundred degrees Celsius and preferably from 10 to 60 degrees Celsius, see column 5, lines 47-50. The reference teaches that the nano materials have dimensions from 0.5 nm to 10 nm and can be solid or fluid –like properties, the nano fluid can be facilitated by the use of high molecular weight surfactant to functional material, see column 9, lines 15-25. Various surfactant described are ethylene and propylene oxides, alcohols, amides and esters, see column 6, lines 45-55.

The reference does not teach adding an aqueous solution of coating material or freeze drying or spray drying.

Westesen et al. discloses an invention relating to the area of administration forms and delivery systems for drugs, vaccines and other bioactive agents. The reference also describes the process of preparing micron and submicron particles of bioactive agents. The process as depicted describes that a solid lipid or bioactive agent or a mixture of solid lipids is melted; stabilizers are added either to the lipid or bioactive agent or to the aqueous phase only depending on their physicochemical characteristics. Stabilizers may also be added or exchanged after homogenization. (abstract).

Drugs or bioactive agents can be melted together with lipid. Solid lipid particles such as fatty acids and their esters are disclosed on column 9, lines 23-25. Various drugs have been disclosed in column 10, lines 30-60. The bioactive agents can be

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dissolved, solubilized and dispersed in the matrix, see column 10, lines 61-64. The reference teaches that drugs or bioactive substances may be melted or may be dissolved, solubilized or dispersed in the lipid melt, see column 11, step (4). The melted lipid compounds are emulsified in the dispersion medium, see step (5) on column 11.

Starch and glucose are taught as stabilizers in column 15, lines 35-38. **Propylene glycol** is taught in column 15, lines 40-45. Glycerol is taught in example 26.

The aqueous phase is heated to the temperature of the melt before mixing and may contain for example, stabilizers, isotonicity agents, buffering substances, and /or preservatives. The molten compounds are **emulsified** in an aqueous phase by **high pressure homogenization (abstract, column 11 and steps 1-8)**. Drugs or bioactive agents particularly suitable are listed in column 10, lines 30-60). Ibuprofen and vitamins are also enlisted on the same column. Further in step 8 in column 11, lines 50-55, it is disclosed that the dispersion medium can be reduced by standard techniques such as **freeze drying and the lyophilized powder** can also be processed into other pharmaceutical formulations such as tablets etc. Regarding the end product being emulsion, the prior art teaches that the melted lipid compounds are emulsified in dispersion medium (see step (5) in column 11 (instant specification , on page 20, teaches in lines 27-28 that the heating step is for very short time such that the emulsion state is present for short time).

The bioactive drugs can be dissolved or crystalline or amorphous or a mixture of these crystallographic states. Role of surfactant is described in example 19 on column 24. Various isotonicity agents such as glycerol or xylitol and sucrose, glucose are

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disclosed on column 10, lines 10-15. The suspensions and lyophilizates can be used for peroral, buccal, pulmonary etc. depending on the particle size (see column 14, lines 40-45). The reference further teaches the importance of smaller particle size during drug delivery process (see column 2, lines 10-25). The reference teaches that the drug carrier systems in the micrometer size range are represented as microspheres which are encapsulated (column 3, lines 30-35). The mean particle size lies in nanometer range and is prepared by emulsion polymerization or by solvent evaporation, see column 3, lines 35-37. The submicron size is of less than 50 nm is shown in column 6, lines 50-53.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the coating materials such as saccharides and utilize the drying process of spray drying as taught by Westesen et al. in to the teachings of Irvin et al. because both the references are directed towards teaching preparation of nanoparticulate formulation fro drug delivery. One of ordinary would have been motivated to utilize the known coating process and known spray drying process of Westesen et al. into the known process of forming nanoscale particles as taught by Irvin et al. Regarding various temperatures and pressures recited in claims 17-25 and claims 32-33, it is the position of the Examiner that one of ordinary skill would have recognized varying temperatures and pressure to optimum degrees since prior art by Irvin teaches utilization of temperature and pressure during nano particle formation of substance. One of ordinary would have envisaged utilizing optimum temperature and pressure limitations in order to obtain nano particulate pulverized particles for drug delivery

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absent evidence of any criticality shown by applicants. Addition of various additives would have been obvious since the references teach addition of sugar, glycerin and stabilizers etc. It is further to be noted that addition of such ingredients are optional as claimed.

4. Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Irvin et al. (USP 7,276,184) in view of Westesen et al. (US Patent No. 5,885,486) and further in view of Rochling et al. (USP 6,602,823).

The references taught above generically teach additives in the preparation. The references do not teach each and every additive claimed in claim 42. Rochling teaches various specific additives that are known to be utilized in the formulations. Rochling teaches dispersants such as gelatin, starch, polyvinyl alcohol, polyvinylpyrrolidone and preservatives in column 6, lines 50-65. Fillers such as carbonates and silicates silica gels in column 7, lines 1-10.

It would have been obvious to one of ordinary skill in the art to substitute specific additives in formulation of the Irvin and Westesen motivated by the teachings of Rochling et al. because these ingredients are known to be added as additional components in pharmaceutical art. It is further to be noted that addition of such ingredients are optional as claimed.

Response to Arguments/Declaration

5. Applicant's arguments filed 03/16/10 have been fully considered but they are not persuasive.

(applicant's arguments are in light of the 37 CFR 1.131 declaration filed by applicants)

Applicant argues that The Irvin reference has a filing date of July 11,2002 and the Westesen reference has a filing date of December 2, 1996. The accompanying declarations under Rule 131 establish that Applicants' invention was made prior to July 11, 2002 and that Applicants continued to diligently pursue the invention and the filing of a patent application from the date of conception through the date their priority application was filed, on October 18, 2002. Applicants refer to prior art documents LEA35177 and WO95/21688. LEA35177 is the assignee's internal docket number and corresponds to WO03/034822. Both WO95/21688 and WO03/034822 are discussed in the specification, and both have been made of record through an IDS submitted April 24, 2008. applicant's therefore assert that the instant invention was therefore completed prior to the effective date of Irvin (US7,276,184), and Irvin is not an effective reference against the present claims. As such the rejection of claims 16-36, 40, 42 and 44-45 16-36, 40, 42 and 44-45 under 35 U.S.C. 103(a) as obvious over Irvin (US 7,276,184) in view of Westesen et al. (US 5,885,486) shall be withdrawn. Regarding claim 42 as discussed above, however, the Irvin reference is not effective against the present claims, and the rejection of claim 42 under 35 U.S.C. 103(a) as obvious over Irvin (US 7,276,184) in view of Westesen et al. (US 5,885,486) and further in view of Rochling et al. (US 6,602,823) shall also be withdrawn.

Applicants arguments in light of declaration are not persuasive because of the following reasons: The declaration filed on 03/16/10 under 37 CFR 1.131 has been considered but is ineffective to overcome the Irvin's reference used in the rejections for the following reasons: Applicant's arguments in light of the declaration are not persuasive because applicants have not provided original exhibits of drawings or records or laboratory notebook papers, pages etc. to show evidence of conception of the invention prior to the effective date of reference coupled with due diligence from prior to said date to a subsequent reduction to practice or to filing of the instant application. Applicants indication that both references WO95/21688 and WO03/034822 are mentioned in instant specification is not sufficient to overcome the rejections based on the 1.131 affidavit filed. As such the declaration filed on 03/16/10 under 37 CFR 1.131 is ineffective to overcome the Irvin's reference used in the rejections. The Examiner refers to MPEP in this context:

715.07 [R-3] Facts and Documentary Evidence

I. GENERAL REQUIREMENTS

The essential thing to be shown under 37 CFR 1.131 is priority of invention and this may be done by any satisfactory evidence of the fact. FACTS, not conclusions, must be alleged. Evidence in the form of exhibits may accompany the affidavit or declaration. Each exhibit relied upon should be specifically referred to in the affidavit or declaration, in terms of what it is relied upon to show. For example, the allegations of fact might be supported by submitting as evidence one or more of the following:

(A) attached sketches;

- (B) attached blueprints;
- (C) attached photographs;
- (D) attached reproductions of notebook entries;
- (E) an accompanying model;
- (F) attached supporting statements by witnesses, where verbal disclosures are the evidence relied upon. *Ex parte Ovshinsky*, 10 USPQ2d 1075 (Bd. Pat. App. & Inter. 1989);
- (G) testimony given in an interference. Where interference testimony is used, the applicant must point out which parts of the testimony are being relied on; examiners cannot be expected to search the entire interference record for the evidence. *Ex parte Homan*, 1905 C.D. 288 (Comm'r Pat. 1905);
- (H) Disclosure documents (MPEP § 1706) may be used as documentary evidence of conception.

Exhibits and models must comply with the requirements of 37 CFR 1.91 to be entered into an application file. See also MPEP § 715.07(d).

A general allegation that the invention was completed prior to the date of the reference is not sufficient. *Ex parte Saunders*, 1883 C.D. 23, 23 O.G. 1224 (Comm'r Pat. 1883). Similarly, a declaration by the inventor to the effect that his or her invention was conceived or reduced to practice prior to the reference date, without a statement of facts demonstrating the correctness of this conclusion, is insufficient to satisfy 37 CFR 1.131.

37 CFR 1.131(b) requires that original exhibits of drawings or records, or photocopies thereof, accompany and form part of the affidavit or declaration or their absence satisfactorily explained. In *Ex parte Donovan*, 1890 C.D. 109, 52 O.G. 309 (Comm'r Pat. 1890).

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday to Friday; 8:30 a.m. to 5:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Snigdha Maewall/

Examiner, Art Unit 1612

/Gollamudi S Kishore/

Primary Examiner, Art Unit 1612